Marine Vertebrates, Cnidarians and Mollusks

L. Keith French and B. Zane Horowitz

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Jellyfish

Jellyfish belong to the phylum Cnidaria (Greek derived from 'nettle') and are mostly free-swimming marine animals that may have an umbrella-shaped bell with varying length tentacles. The pulsations of the bell are relied on as their mode of locomotion, while the tentacles are typically used for capturing prey. Jellyfish have a worldwide distribution, occupying every ocean and some freshwater lakes. The phylum is comprised of several distinct life forms and four important classes of jellyfish: Cubozoa, Hydroza, Anthozoa, and Scyphozoa. The defining feature of Cnidaria is the cnidocyte, and the tentacles of most jellyfish are lined with thousands of them (Figs. 1 and 2). Each cnidocyte contains a harpoon-like organelle known as a cnida or cnidocyst. On the external surface of the cnidocyte is a cnidocil which, when activated by pressure, osmotic, or chemical changes, acts like a trigger, releasing the previously coiled harpoon. Once forcefully expelled, a process that takes microseconds, the harpoon is capable of penetrating human tissue. Venom is forced out of the cnidocyte under pressure through the epidermis and upper dermis and, particularly if dermal capillaries are inoculated directly, can enter the systemic circulation. It is sometimes stated that these may be inadvertently accelerated by the rubbing or shaking of a startled human victim, but there is no reliable evidence that this actually occurs.

The Cubozoa, or box jellyfish, are not considered true jellyfish, but represent the phylum's most dangerous species (*Chironex fleckeri*, *Malo kingi*, *and Carukia barnesi*). This class contains cube-shaped, four-cornered jellyfish that are ordained with up to 15 tentacles per corner. *Chironex fleckeri* (roughly translated from Greek as the "assassin's hand") is commonly referred to as the big box jellyfish. This species of jellyfish is endemic to Australia, particularly off the Northern Coast [1]. As an adult the *C. fleckeri* has a bell the measures up to 38 cm with tentacles that may reach 3 m in length. The much smaller *Carukia barnesi* (family *Carybdeid*), aka "Irukandji jellyfish," which as an adult, has a bell that measures a mere 2.5 cm in diameter and tentacles the reach up to 100 cm from the bell. Given its small size, this jellyfish is not only elusive to the unsuspecting swimmer, but historically proved elusive to investigators. Hugo Flecker originated the term "Irukandji syndrome" in 1952 which is used to describe a set of clinical manifestations associated with, though not specific to, the sting of *Carukia barnesi* [2]. While its range was initially thought to be fairly wide, the "Irukandji jellyfish" is probably limited to Queensland waters [2] and the assumption of a wider distribution may be from envenomations from other members of the carybdeid family (i.e., *Carukia shinju*).

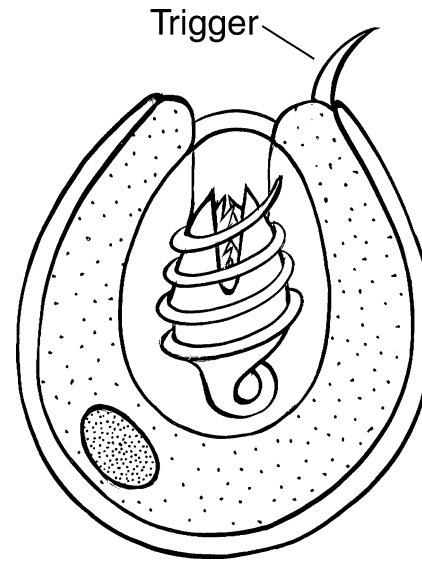

Fig. 1 Nematocyst before discharge (From Ref. [133], p. 1454)

Interestingly, in 1964 a volunteer lifesaver by the name of Barnes cemented his place in history when he captured a specimen of a previously unnamed jellyfish and intentionally stung himself, and his own son, who were treated on site and survived. The offending jellyfish was named *Carukia barnesi*, sometimes referred to as the "Barnes' jellyfish" [3]. Despite the lore around this species of box jellyfish, there has only been one death worldwide attributed to its sting.

Malo kingi (formerly *Chiropsalmus quadrigatus*), a species of box jellyfish, is also found in the Indo-Pacific region, particularly off

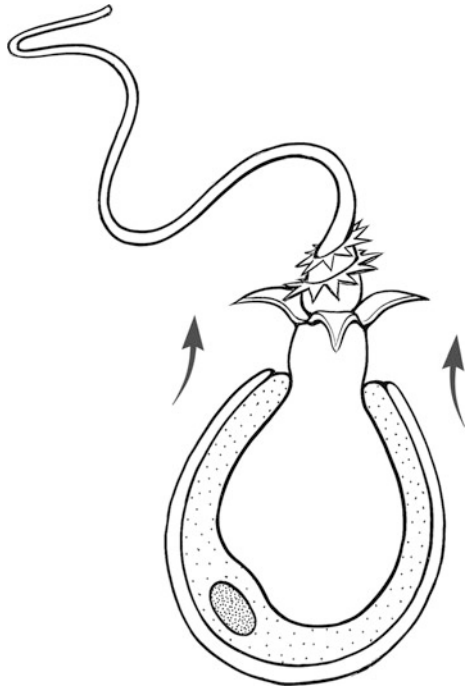

Fig. 2 Nematocyst after discharge (From Ref. [133], p. 1455)

the Philippian coast. This species has a bell measuring 7 cm in diameter and may have upwards of 60 tentacles, reaching as long as 3 m.

The Hydrozoa class contains two important species of jellyfish (*Physalia physalis* "Portuguese Man O'War" and *Physalia utriculus* "Pacific Man O'War") and several species of medically important organisms (discussed below). An interesting feature of these two jellyfish is that rather than being a single self-sustaining organism, the creatures are a mass of hydroids living as a single colony. The floating colony is easily recognized by the characteristic sail, usually blue, which floats above the water's surface. These hydrozoa can be found anywhere on the open ocean, but are more commonly found in tropical/subtropical regions of the Atlantic, Indian, and Pacific Oceans.

Scyphozoa, or true jellyfish, are home to a few medically important jellyfish such as *Cyanea capillata* (lion's mane jellyfish), *Chrysaora quinquecirrha* (sea nettle), and *Linuche unguiculata* whose larvae may cause a condition known as sea bather's eruption. *Cyanea capillata* is considered one of the longest animals in the world, its combined length of the tentacles reaching as long as 63 m. Both *Cyanea* and *Chrysaora* spp. are found in tropical and temperate waters including, in particular, the Chesapeake Bay.

Pharmacology

Cnidaria venom is a complex, proteinaceous mixture capable of causing dermatonecrosis, myonecrosis, and cardiotoxicity and is species dependent.

Chironex fleckeri is considered one of the most venomous creatures in the world [4]. In 1959, Southcott and Kingston described a triad of basic toxicologic manifestations, cardio-respiratory failure, dermatonecrosis, and hemolysis. Over the last five decades, further in vitro and in vivo animal research has provided some insight into the reasons why certain clinical features are observed. First, a biphasic blood pressure response (initial hypertension, then hypotension) is often observed. An initial vasoconstrictive phase is followed by subsequent hypotension, likely from reduction in coronary blood flow, heart rate and contractility, arrhythmias, and baroreceptor stimulation [5]. Furthermore, there is an irreversible increase in intracellular calcium in rat myocytes which is speculated to correlate to atrioventricular block and systolic dysfunction in human cardiac tissue. This ion influx may result from pore-forming properties from two of *Chironex fleckeri's* most abundant venom components, CfTX-1 and 2 [6].

The pain following envenomation may arise from modulation of nonselective cation channels expressed in nociceptive neurons [7]. There at least two myotoxins in the venom, both of which are capable of inducing skeletal muscle contractions in rat models [8]. Hemolytic effect, which may be a surrogate marker for venom-induced cell-permeability and ion pore formation, is a rarely reported finding in humans [4].

Carukia barnesi is capable of inducing "Irukandji syndrome," a series of signs and

symptoms common in excess catecholamine states. Crude venom extract has been shown to cause the release of catecholamines in both in vitro and in vivo experiments [9]. The catecholamine release is likely, at least in part, from a prejunctional neuronal sodium channel activator which may be attenuated in the presence of tetrodotoxin or conotoxin. There is also, however, concentration-dependent contraction in rat mesenteric arteries that is not inhibited by tetrodotoxin. In isolated, human right atrial muscle, exposure to crude venom extract initially reduced contractile force, but was followed by a more sustained force of contraction. Sustained tachycardia and pulmonary hypertension has been demonstrated in in vivo piglet experiments where elevations of circulating noradrenaline and adrenaline were measured [9]. Winkel et al. have also noted that while the clinical manifestation is that of sympathetic nervous system activation, parasympathetic activation may play a role in the overall autonomic dysregulation that occurs following envenomation.

In vivo and in vitro studies on *M. kingi*, a box jellyfish smaller than *C. fleckeri*, have demonstrated extra-cellular calcium-dependent vasoconstriction and positive ionotropic actions, which, at high concentration, become cardiodepressive [10–12].

Physalia physalis venom contains numerous proteins capable of myriad effects. Physalitoxin, a potent hemolysin, compresses about 28 % of the total protein composition of the venom [13]. The venom most likely damages target cells by insertion into plasma membranes with subsequent pore formation, potassium efflux, and colloid osmotic lysis [14]. Intracellular calcium influx, induced through toxin induced pore formation, may occur at in vitro exposure as low as 10 ng/ml [15]. The influx of calcium is associated with a release of intracellular lactate dehydrogenase (LDH). In a canine model, intravenous administration of *Physalia physalis* venom induced arrhythmias, hypertension, hyperkalemia, hyponatremia, and hemolysis [16].

Pathophysiology

Chironex fleckeri is probably the most medically important jellyfish and is one of the most dangerous animals on the planet. Reports are variable, but over 70 deaths have been reported from *C. fleckeri* envenomation [17]. Swimmers may not observe the jellyfish prior to or even after a sting. Most stings are innocuous and prospective studies have demonstrated that the majority of victims will not experience life-threatening symptoms [18]. For severe envenomations, symptoms begin with severe, unrelenting pain. Autonomic dysfunction, manifest as hypertension, may progress to hypotension, apnea, and cardiovascular collapse. Dysrhythmias have been reported in piglet models [5]. Coma may occur after the sting, which, when in the marine environment, may lead to drowning. Death is more likely if the length of cutaneous exposure exceeds 3 m [19].

Carukia barnesi is capable of inducing the "Irukandji syndrome." In fact, *C. barnesi* was once referred to as the Irukandji jellyfish, but other members of the carybdeid family (*M. maxima, C. shinju*) are also capable of inducing this syndrome. Like envenomation from *C. fleckeri*, the victim of a *C. barnesi* sting may never see the offending organism. The sting is generally felt within a few moments of contact. The pain is not usually as severe as that of the big box jellyfish. Systemic features may begin within minutes and are manifest as muscular pain (in particular low back) and cramping (abdominal wall and limb), vomiting, diaphoresis, agitation, and hypertension [2]. In one case series, the symptom/sign frequency was abdominal cramps (40 %), hypertension (50 %), back pain (39 %), nausea/vomiting (39 %), muscular cramping of the limbs (34 %), chest tightness (26 %), and distress (24 %) [20]. Troponin elevation, EKG abnormalities, and echocardiographic findings ranging from mild systolic dysfunction to global myocardial dysfunction were reported in another large series of *C. barnesi* envenomations [21]. Fatal intracranial hemorrhage has been reported in one case of an extreme sequela of envenomation [22].

Envenomation from *Malo kingi* is reported to occur hundreds of times annually with at least three reported deaths [23]. The jellyfish can be found throughout the Indo-Pacific region, but is more commonly reported around the Philippines and Japan. Contact with *Malo kingi* is generally less severe than that of *C. flexeri*, though immediate, severe pain, cardiovascular collapse, and pulmonary edema are described [17].

Physalia physalis envenomations are common occurrences along the Atlantic Coast of the USA but are not limited to these waters and cause major stings worldwide. Symptoms of envenomation are generally immediate and localized, but delayed symptoms and systemic features can occur. Common symptoms include localized pain (mild to severe) and paresthesias and often accompany a linear, papular, or bullous rash or urticaria. Systemic features include diaphoresis, tachycardia, nausea, vomiting, muscle pain, headache, chills, and transient paralysis of the affected limp [24]. Hemolysis and renal failure has been reported [25]. Immediate, severe pain/distress followed by apnea and cardiac arrest has been reported (Irukandji syndrome) [26].

Dermatologic effects from jellyfish envenomation may arise from distinct toxins. Immediate dermatitis, skin discoloration, and local pain are the most common syndromes following cnidarian envenomation [27]. The local immediate and persistent wheals following sea nettle stings are likely an effect of leukotrienes, histamine, and neutrophil chemotactic activity [28]. Prolonged lymphokine responses have been demonstrated following jellyfish antigens, suggesting a T cell function may be a driving factor in the pathogenesis of skin lesions [29]. Erythema nodosum has been reported following a sting from *Physalia physalis* [27].

Clinical Presentation and Life-Threatening Complications

The majority of people envenomated by jellyfish will experience mild to moderate pain with or without cutaneous manifestation. Many victims may never seek medical attention. Nonspecific symptoms include nausea/vomiting, diaphoresis, and malaise. The severity of the toxidrome is variable and marked most commonly by dermatologic, cardiopulmonary, and neurologic effects.

Dermatologic manifestation can include skin discoloration, bullae, and urticaria. The clinical findings following contact with *C. fleckeri* are reported to be "distinctive" and described as heavily marked in a crisscross pattern, with transversely barred wheals which may be 8–10 mm wide ('frosted ladder') [17] (Fig. 4a, b). Delayed hypersensitivity reactions, characterized by a maculopapular rash, can occur 1–2 weeks after exposure. Necrosis of the skin can occur (Fig. 3 and 4).

Cardiovascular effects may include tachycardia, hypotension, and cardiogenic shock.

Neurologic manifestations generally begin with localized pain at the site of envenomation. Headaches, syncope, vertigo, ataxia, and altered mental status (agitation, delirium) may occur. Local paresthesia and transient limb paralysis are reported after *P. physalis* stings [24]. One death from intracerebral hemorrhage has been described following envenomation from *C. barnesi* [22].

The "Irukandji syndrome" is a serious form of envenomation from the carybdeid family of jellyfish, most notably *C. barnesi*. The syndrome begins rapidly, usually within 30 min, and consists of severe muscle pain/cramps, vomiting, diaphoresis, agitation, hypertension, and potentially acute heart failure or intracranial hemorrhage. Toxin-induced neuronal sodium channel

Fig. 3 Incipient necrosis and blistering within 24 h of box jellyfish (*Chironex fleckeri*) envenomation (Courtesy of John Williamson, MD. From Ref. [133], p. 1469)

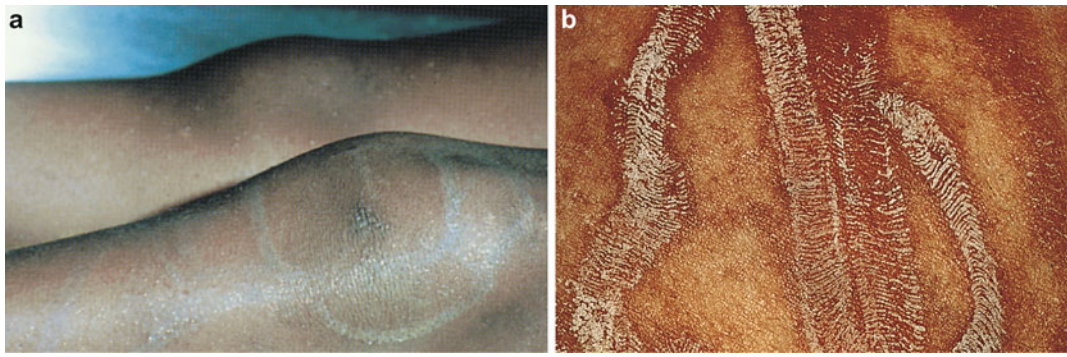

Fig. 4 (**a**) Frosted crosshatched pattern pathognomonic for a box jellyfish envenomation. The victim of this sting died rapidly. (**b**) The enhanced frosted appearance is a result of application of a spray of aluminum sulfate (Courtesy of John Williamson, MD. From Ref. [133], p. 1469)

modulation leading to excessive catecholamine release is the postulated mechanism for this toxidrome [2].

Diagnosis

The constellation of sudden severe pain in a swimmer/bather/diver with cutaneous findings is suggestive of a jellyfish envenomation. Visualization of the jellyfish is obviously a helpful diagnostic clue; however, the small size or transparency of some species may limit visual detection. Examination of shed tentacles left on a victim may be a helpful work up to definitively identify a jellyfish sting, otherwise skin scrapings may be helpful for identifying the species of jellyfish responsible for the toxidrome. Diagnostic tests should be used to identify/follow potentially serious effects from the envenomation (i.e., serial troponins, EKG, echocardiogram, head CT, creatinine).

Treatment

As all envenomations will occur while the victim is in the water, first priority should be to remove the person from the marine environment and onto land or a boat to avoid drowning. There is a lack of data, suggesting a benefit to pressure dressings, and some in vitro evidence, suggesting a harmful effect [30]; therefore, there is no support for their routine use. Patients should be kept calm and still, if possible. Physically removing tentacles should take place, but cautiously. Seawater irrigation and using an instrument to remove the tentacles is often suggested, but there are no data to support this. Health care workers need to don protective gear until complete decontamination is achieved. Tetanus prophylaxis is generally recommended when applicable (i.e., previously unvaccinated or out of date), although these envenomations do not pose a tetanus risk.

There is an exhaustive list of chemicals anecdotally used to neutralize undischarged tentacles left on the bodies of victims. There is no uniform approach or consensus on the protocol for such treatment, and evidence is often lacking or conflicting regarding topical neutralization. A 5 % solution of acetic acid has been suggested to reduce nematocyst discharge from *C. fleckeri* and *C. barnesi* [31] envenomations. There are conflicting reports regarding the benefit of acetic acid for *P. physalis*. Some reports describe pain relief after the topical application of acetic acid [32], while others report immediate nematocyst discharge in both *P. physalis* and *C. quinquecirrha* [33]. Hypotonic solutions (fresh water), ethanol, isopropyl alcohol, and meat tenderizer are not likely beneficial and may increase nematocyst discharge and therefore should be avoided. Aluminum sulfate surfactant (Stingose [Pfizer], West Ryde, Australia) has been shown to reduce pain following *P. physalis*

[32]. Lidocaine 4 % topical solution with or without acetic acid reduced nematocyst discharge from *C. quadrumanus* and *C. quinquecirrha*. Heat application has been used to treat Irukandji syndrome and has been shown to reduce pain following Physalis *spp*. and *C. alata* envenomations [34]. Parenteral opiate analgesia may be the only necessary intervention to control pain.

The only currently available antivenin for jellyfish envenomation is the Box Jellyfish Antivenom (Commonwealth Serum Laboratories, Melbourne, Australia) (Fig. 5). Indications for treatment include envenomation from *C. fleckeri* with manifestations of systemic envenoming or in those who have extensive local involvement causing extreme pain which does not respond to routine analgesic therapy. Each vial contains 20,000 units of antivenin, and current treatment recommendations are to administer 1–3 vials (same dosing for adults and children) intramuscularly or intravenously (preferred when feasible), though it has been suggested that higher doses may be required to achieve venom neutralization [4, 35, 36]. There also seems to be a time-dependent component to efficacy, with studies indicating that antidote efficacy may be augmented with a prophylactic approach rather than waiting for symptoms to occur [35]. This approach is problematic because most envenomations are mild, and the antivenin is derived from animal plasma; thus, there is a risk for anaphylaxis and serum sickness. Anaphylactic reactions should be treated in the standard manner. Human randomized trials are lacking, and the use of the box jellyfish antivenin remains a controversial point.

Fig. 5 Box Jellyfish Antivenom (Courtesy of John Williamson, MD. From Ref. [133], p. 1470)

Management of serious Chironex envenomations, using verapamil, a calcium channel blocker and smooth muscle relaxant, is controversial and potentially harmful. While some studies have found that death was delayed in mice treated with verapamil before and after administration of venom [37] and lethality could be reduced from 21 of 21 to 16 of 22 mice treated with venom obtained from tentacle extract [38], others have shown that verapamil failed to prevent any effects of the venom and worsened cardiovascular collapse and increased mortality [5]. Currently, it is not recommended to use verapamil in the seriously envenomated patient [17].

There is no specific antidote for "Irukandj syndrome." Painful toxidromes can be managed with opiate analgestics, usually parenterally. The "Irukandj syndrome" may exhibit direct myocardial effects; therefore, fentanyl may be a reasonable opiate to start with (pure narcotic receptor action without myocardial effects or toxic metabolites) [20]. Intravenous magnesium has been used in cases of severe envenomation and has a theoretical advantage because it may decrease vascular resistance in hyeradrenegic states [2]. In one case series, blood pressure reduction and pain improvement were observed in patients treated with IV magnesium (10–20 mmol boluses) [39]. However, a randomized trial comparing IV magnesium to placebo in the management of Irukandji syndrome failed to prove a benefit [40]. Though not without controversy, the authors of this randomized trial suggested reconsideration of the use of magensium in the management of Irukandji syndrome. The Box Jellyfish Antivenom is not expected to provide benefit from carybdae

jellyfish envenomations causing the "Irukandj syndrome," and given the potential harm, it should be avoided if the culpable jellyfish is known. Phentolamine and nitroglycerine have been used in case reports to treat the severe hypertension associated with this syndrome. Cardiovasuclar collpase may require inotropic support and pulmonary edema should be treated in the standard fashion. Patients who are asymptomatic without medications for 6 h after exposure may be discharged home with follow-up and careful discharge instructions.

With Physalia *spp*, there is also no specific antidote. Treatment is supportive with focus on decontamination and pain control. As mentioned previously, there is conflict regarding the use of acetic acid, but given the concern for increasing nematocyst discharge, acetic acid might be best avoided. Though not well studied, severe muscle spasm may respond to 10 % calcium gluconate (5–10 mL slow intravenous push), diazepam, or methocarbamol [25, 41]. Delayed cutaneous reactions, which may coincide with fever, weakness, join pain/stiffness, can be managed with a 10- to 14-day oral prednisone taper starting at 1–2 mg/kg/day [42]. Topical anesthetics, such as benzocaine spray and lidocaine ointment and oral antihistamines, may be soothing.

Since the majority of patients who suffer jellyfish envenomation will experience only mild symptoms, most patients will be appropriately discharged from urgent care or emergency department settings. Hospital, and more specifically intensive care admission, should be reserved for those patients who experience the life or limb threatening problems. This applies to situations where a severe toxidrome requires: Box Jellyfish Antivenom, high dose opiates where respiratory compromise is a concern, evidence of ongoing ischemia (i.e., troponin elevations), intracranial hemorrhage, need for mechanical ventilation, malignant hypertension and end-organ injury, pulmonary edema, anaphylactic reactions, acute heart failure or following resuscitation from cardiopulmonary arrest.

Other Hydrozoa

Approximately one-third of the 10,000 species within the phylum Cnidaria belong to the class Hydrozoa. The medically important hydrozoans are Millepora *spp.* (fire corals), Physalis spp. (discussed above in the jellyfish section), and *Lytocarpus spp* (fire weed or fern weed).

Fire corals are found in the tropical and subtropical waters of the Caribbean Sea and Indian, Pacific, and Atlantic Oceans. They tend to habitat in shallow water. Nematocysts found on tentacles which protrude from pores of the coral can envenomate divers and swimmers who may mistake the fire coral for rocky structures. Fire coral often have brightly colored structures and are brittle and thus easily fracture.

Pharmacology

At least 13 different species *of* Millepora exist and there are reports of various toxic components. Purified components of *M. alcicornis* and *M. tenera* have been shown to elicit hemolytic and dermonecrotic effects [43, 44]. Millepora cytotoxin-1 (MCTx-1), from *M. dichotoma var. tenera*, was the first proteinaceous toxin to be characterized [45]. MGTx-1 belongs to the dermatopontin family and is cytotoxic and hemotoxic in animal studies. Phospholipase A2, isolated from *M. complanata*, is a vasoconstrictive and hemolytic compound in rats [46]. Milleporin-1, a distinct toxin from MCTx-1, has been isolated from *M. platyphylla* and is also hemolytic to human red blood cells in vitro [47].

Clinical Presentation and Life-Threatening Complications

Contact with *L. philippinus* induces painful and pruritic wheals. Symptoms following contact with fire coral generally begin within 30 min of contact. There is often burning and stinging at the site of contact. A pruritic, erythematous,

Fig. 6 Hydroid sting on arm of a diver (Photo by Neville Coleman. From Ref. [133], p. 1461)

Fig. 7 Fernlike hydroid print on the knee of a diver (Photo by Paul Auerbach, MD. From Ref. [133], p. 1461)

vesicular, or raised rash develops soon afterward. Violaceous papules and plaques may be replaced by blisters once resolved [48] (Figs. 6, 7 and 8). Though brittle, the backbone of the fire coral is sharp enough to cause lacerations or local trauma to the skin of those who contact it. Allergic and anaphylactic reactions would be suggested if systemic symptoms such as angioedema, bronchospasm, or diffuse erythema develop. Like all wounds from marine sources, secondary infections can occur. There is at least one case report of delayed nephrotic syndrome, pulmonary edema, and renal failure following exposure to fire coral [49]. Contact with *M. dichotoma* was reported to cause a full-thickness burn requiring admission to a burn unit [50].

Fig. 8 Fire coral sting (Photo by Kenneth Kizer, MD. From Ref. [133], p. 1462)

Diagnosis

There is no routine or specific diagnostic testing to confirm fire coral or fire weed stings. The differential diagnosis would include jellyfish stings or trauma from non-Cnidaria coral. There is no role for routine diagnostic testing to investigate systemic injury in the context of minor, local symptoms. However, if systemic features occur, renal function testing, chest radiography, and complete blood counts may be beneficial.

Treatment

Like treatment for jellyfish stings, treatment for fire coral or fire weed envenomations begins with removal from the water environment. Rescuers should put on gloves and carefully remove any remaining tentacles with an instrument such as forceps. The skin should be rinsed with salt water. Hot water immersion may be helpful in control of pain (Table 5) Acetaminophen or non-steroidal anti-inflammatory medications are generally sufficient enough to treat the pain associated with the sting, though in severe cases, opiates may be indicated. Application of ice packs is recommended for *L. philippinus* stings, but not dousing with urine, vinegar, or methylated spirits as these may increase nematocyst discharge [51]. Topical steroids and oral antihistamines reduced the severity of symptoms, but not skin manifestation in one case series of Red Sea Coral

stings [48]. Allergic reactions and anaphylactic reactions should be treated in the standard fashion. In the reported case of nephrotic syndrome, a single-dose intravenous methylprednisolone (120 mg), followed by oral prednisone (75 mg/d), was used [49]. Surgical debridement may be necessary if necrosis complicates the dermal effects. Tetanus prophylaxis should be employed in the appropriate circumstances.

ICU admission is indicated in the rare instance of severe anaphylaxis, sepsis complicating envenomation, or pulmonary edema.

Stingrays

Stingray point in the US state of Virginia gets its name from an event that occurred during Captain John Smith's exploration near Jamestown. He sustained a serious stingray injury while exploring Chesapeake Bay near the Rappahannock River, but he recovered and later ate the stingray for dinner (Stingray Point historic marker N 76).

Stingrays inhabit the oceans, bays, inlets, and rivers of temperate and tropical climates around the world [52]. Rivers around the world with species of stingrays include the Amazon, Niger, Mekong, and those in Australia [52–54]. Stingrays are flat fish that have wide muscular wings to swim, but they often burrow into sandy ocean bottoms and await their prey. They are cartilaginous similar to sharks; however, they will not attack or pursue a human diver or bather, and most injuries occur when they are accidentally stepped upon and the stingray reflexively flex their whip-like barbed tail producing a deep penetrating injury likened to a knife wound [53].

Some 2000 stingray injuries occur in the USA each year and many more worldwide [52]. One of the more tragic occurrences was the 2006 death of Steve Irwin, an Australian naturalist and TV personality known as the "Crocodile Hunter," when he sustained a cardiac wound from a stingray, emphasizing how quickly these encounters can turn deadly. His was not the first such fatal cardiac wound reported, a young woman died in New Zealand from a similar wound in 1939

Table 1 Stingray families

True stingrays	True rays
Dasyatidae (Whiptail stingrays)	*Myliobatidae* (Eagle rays, Manta rays)
Urolophidae (Round stingrays, "stingarees")	*Gymnuridae* (Butterly rays)
Potamotrygonidae (Freshwater stingrays)	*Rhinopteridae* (Cow nose rays)

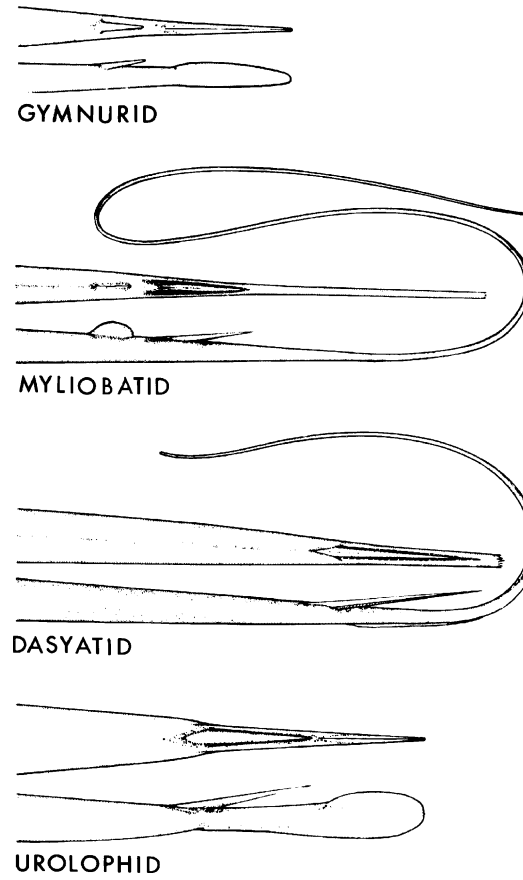

Fig. 9 Four anatomic types of stingray venom organs (From Ref. [133], p. 1489)

[53]. A report in 1988 described a 12-year-old boy who sustained a penetrating chest wound from a stingray, received medical care, but died 6 days later at home from sudden cardiovascular collapse due to pericardial tamponade [54].

Stingrays, and the less injurious rays, are represented by 150 species within three families (Table 1). Each family has a distinguishing tail

with one to four serrated spines (Fig. 9). The most dangerous is the *Dasyatidae* family due to the location of the spine and the length (37 cm) of its tail increasing penetrating efficiency [52]. This sharp serrated spine, with rear-facing barbs, acts like a knife that can impale itself in a human when the stingray is disturbed and then reflexively arches its tail in self-defense. The spines often break off in the victim, but this does not kill the stingray. The spine can penetrate neoprene boots worn by divers. The spine's sheath contains two longitudinal grooves that contain venom [52].

Pharmacology

The venom is poorly characterized but contains 5′-nucleotidase, phosphodiesterases, and other tissue spreading factors [52]. Some as yet uncharacterized component of the venom may have direct cardiotoxicity [52, 55].

Clinical Presentation and Life-Threatening Complications

Stingrays inflict a penetrating wound from which the barb spine cannot be easily removed. The venom itself has low toxicity but plays a role in the inflammatory response and pain felt at the wound site [52]. Wounds to the heart, liver, spine, femoral artery, and extremities have been reported [52–54, 56–60]. Potential complications include cardiac tamponade and internal bleeding, and the victim may present in decompensated shock requiring emergent resuscitation. Arrhythmias possible due to the venom in the absence of a cardiac wound have been reported [55]. The most common wound from stepping on a stingray is a wound to the foot or lower leg (Figs. 10 and 11). Pain from any of these wounds is often excruciating and lancinating in character, peaking in 15–90 min and lasting up to 2 days [52]. Pain can extend up the entire limb, and a variety of systemic effects including nausea, vomiting, seizures, muscle spasms to the degree where the individual cannot continue to swim, and hypotension may occur [52].

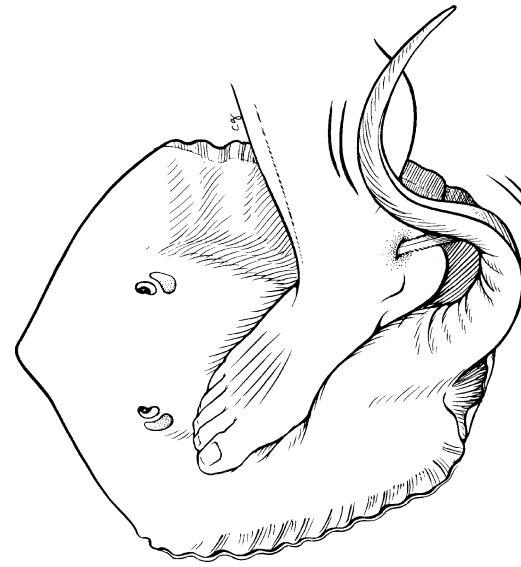

Fig. 10 The stingray lashes its tail upward into the leg and generates a deep puncture wound (From Ref. [133], p. 1490)

Treatment

Critical attention to the resuscitation from penetrating trauma is the key management for stingray injuries. Injuries to the head or torso may require airway management, fluid resuscitation, and potential need for chest thoracostomy or operative exploration in an operating room. Embedded chest and abdominal spines should not be pulled out blindly. Extremity injuries should be evaluated for vascular and nerve lacerations. Pain control in a stable patient will require immersion of an affected limb in hot water (45 °C/113 °F) [52]. Wounds may appear cyanotic centrally. Wounds should be both x-rayed and explored for retained foreign bodies which should be removed. Plain radiography may miss these thin spine structures, and direct wound exploration is mandatory [60]. Often local or regional anesthesia is need to achieve adequate wound exploration and debridement [52]. Antibiotics are usually given for penetrating traumatic injuries from the marine environment and should be broad-spectrum to cover for organisms such as *Vibrio damsela* (now *Photobacterium damsela)* [52, 61]. Penetrating wounds to bowel should

receive antibiotics to cover gram-negative and anaerobic bacteria.

Delayed complications from these wounds may include risk of cellulitis, septic arthritis, necrotizing fasciitis, and osteomyelitis. A pseudoaneurysm of the superficial femoral artery has been reported [62].

Fig. 11 Stingray spine tip broken off into the heel of a victim (Photo by Robert D. Hayes. From Ref. [133], p. 1490). See Color Fig. 11

Scorpaenidae

The bony fishes of the family Scorpaenidae (Table 2) represent a diverse group of fish, from both freshwater and seawater habitats throughout the world (Fig. 12). They all have a bony plate across their back from their eye to their gill, with spines that cover a venom gland. When pressure is applied to these spines, as when the fish is stepped on, they release their venom into the wound created by the sharp spine. A few species have importance in human envenomation, the most severe of which is the stonefish. Other species of spiny fish have also been implicated in less common instances of envenomation (Table 3).

The stonefish are the most toxic of this group of marine envenomations. These are bottom-dwelling fish, which have a natural camouflage to appear like a rock or coral. Additionally they can burrow into sand and lay motionless for long periods of time so to give the appearance to an inattentive diver that they are part of the coastal rocky bottom. At times algae overgrowth on their skin adds additional camouflage to their appearance. Most stone fish are found between the Tropics of Cancer and of Capricorn in Australian coastal waters, in the Indian and Pacific Oceans. They do not naturally live along North American shorelines. While envenomation can cause hypotension, muscle paralysis, acute pulmonary edema, and cardiac dysrhythmias, it is not usually lethal. Although some resources claim that stonefish envenomation could potentially be fatal, the only fatality in Australia is that of Dr. Joseph Wassell, which occurred in 1915 on remote Thursday Island in the Northern Territories

Table 2 Scorpaenidae: bony fishes

Synanceja: Pacific and Indian Oceans, North or Tropic of Capricorn	*Scorpaena*: Pacific and Atlantic Oceans, Caribbean Sea	*Pterois*: Pacific Ocean including North American West Coast
Stonefish (*Synanceia verrucosa)*	Scorpionfish (*Scorpaena plumieri*)	Lionfish (*Pterois volitans, also*: *Pterois radiata*, and *Pterois russellii*)
Indian Stone fish *(Synanceia horrida*)	Soldierfish (*Gymnapistes marmoratus*)	Turkeyfish (*Pterois mombasae, Pterois sphex*)
Australian estuarine stonefish *(Synanceia trachynis)*	Sculipin: (*Scorpaena guttata*)	
Midget Stonefish (*Synanceia alula*)	Bullrout (*Notesthes robusta)*	
Red Sea Stonefish (*Synanceia nana*)	Red Rock Cod *(Scorpaena ergastulorum)*	

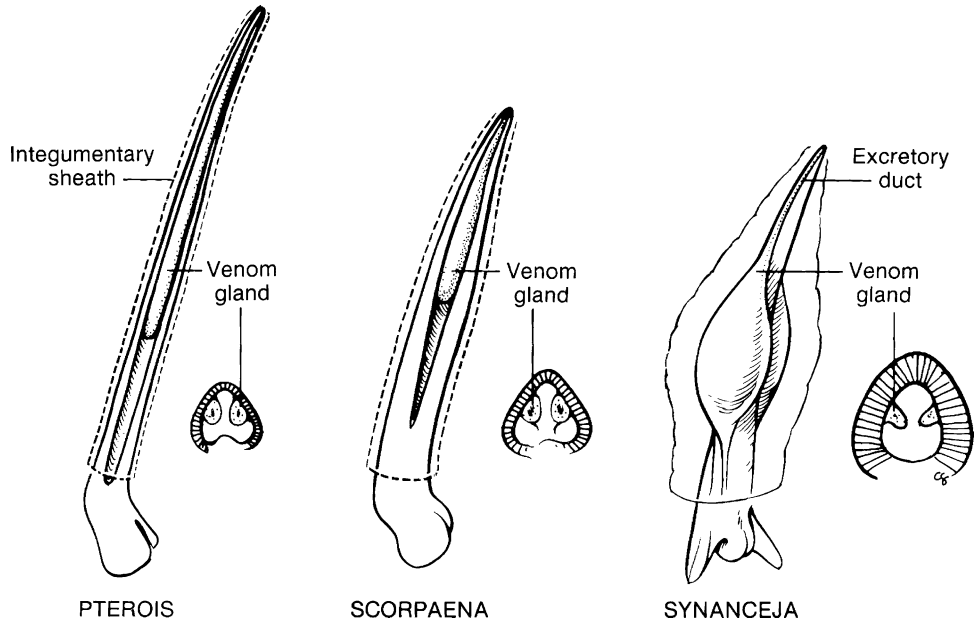

Fig. 12 Lionfish, scorpionfish, and stonefish spines with associated venom glands (From Ref. [133], p. 1495)

Table 3 Other spiny venomous fish

Thalassophryne nattereri (Atlantic Toadfish)
Thalassophryne maculosa (Cano Toadfish)
Hydrolagus colliei (Pacific Ratfish)
Chimaera monstrosa (European Ratfish)
Kathetostoma averruncus (Stargazer)
Scatophagus argus (Spotted Scat, Butterfish)
Selenotocota multifasciata (Silver Scat, Stripped Butterfish)

[63]. Two other fatalities occurred in the Indian Ocean in the Seychelles and on Mozambique in the 1950s [63]. With modern supportive care, envenomations from this group of marine life are treatable and victims should survive with access to medical care [64].

There are over 80 species of *Scorpaena*, but only a few have documented human envenomations, and none have been lethal. Like stonefish they are well camouflaged. They are in both the Pacific and Atlantic Oceans and are one of the most common venomous fish along the coast of Brazil [65]. The venom apparatus varies between species that may possess 10–15 dorsal spines, and 2 pelvic and 3 anal spines, each with venom glands.

The least toxic of the scorpaenidae group are the lionfish (*Pterosis spp)*, which go by a variety of names including zebrafish, dragonfish, firefish, and turkeyfish [66–70]. They are endemic to southern hemisphere coral waters but have been introduced in the Atlantic and Caribbean and are considered an invasive species along the US East Coast [71]. These are a favorite for aquarium hobbyists, as they are free-swimming fish with thin ornate spines and coloration. In aquarium owners, they have been responsible for envenomations of the hands and fingers due to efforts to handle the fish or clean the aquarium [66–68]. Even handling a lionfish which had been dead for 1 or 2 days can result in envenomation [66].

Pharmacology

The venom apparatus is contained in its grooved dorsal spines and pelvic and anal spines. The spines are covered with an integumentary sheath over a venom gland. Each venom gland may contain 5–10 mg of venom [64, 72]. These venoms present a complex mixture of substances

when injected into the skin, but the end result is severe pain, tissue destruction, hemolytic activity, and systemic effects. Components of the venom include hyaluronidase as a tissue spreading factor, and the toxic components, stonustoxin, verrucotoxin, and trachynilysin. Stonustoxin, a heat-labile protein purified from *Synanceia horrida,* is composed of alpha and beta subunits and has a molecular weight of 148,000 Da [72, 73]. In animal models, stonustoxin causes hemolysis and edema, through local vasodilation, but this is generally not seen in human envenomations [72]. Verrucotoxin, from *Synanceia verrucosa*, has two alpha and two beta subunits, with a molecular weight of 322,000 Da [74]. The beta subunit has a 96 % homology with the beta subunit of stonustoxin [72–74]. Verrucotoxin inhibits calcium and activates potassium channels in frog atrial tissue, but human cardiac effects are rare [74]. Trachynilysin, from *Synanceia trachynis*, has a molecular weight of 158,000 Da. It causes release of acetylcholine at the neuromuscular junction and causes negative inotropy and cholinergic effects, possibly through calcium influx [72–74]. Other vasogenic amines norepinephrine, serotonin, dopamine, and tryptophan, and enzymes acetylcholinesterase, phosphodiesterase, arginine esterase, and 5′-nucleotidase are also present in these venoms [64].

Clinical Presentation and Life-Threatening Complications

When a stonefish is stepped on, and a diver is envenomated, the clinical effects include severe pain, which peaks within 60–90 min after envenomation, and may persist for up to 12 h [72–76]. It is often described as severe burning in nature [76]. Other symptoms may include headache, muscle aches, diaphoresis, vomiting, diarrhea, restlessness, delirium, seizures. A variety of both tachydysrhythmias and bradydysrhythmias have been reported, as have acute pulmonary edema, hypotension, syncope, and pericarditis [75, 76]. The wound is painful, may bleed due to venom components with anticoagulant activity, and will appear cyanotic or ischemic centrally with a perimeter of erythema [64]. Local vesicles and bullae may form, and local lymphangitis may occur. Wound healing is very slow, taking months to heal, with possible secondary complications such as deep abscess formation, granuloma formation, and neuropathy.

Envenomation from the *Scorpaena* species, and related spiny fish, causes similar signs and symptoms as stonefish but are less severe. Since some of these species, such as sculpin, are harvested for food, hand injuries in fisherman are more common in this group of fish. In rat models of envenomation, hypertension and tachycardia occur first, followed by vasodilation, hypotension, and bradycardia prior to death [77]. Some other species such as bullrout and soldierfish are often grouped with these fish as potential venomous species [77–80]. Stonefish antivenom has been shown in vitro and in animal models to have activity for some *Scorpaena* and soldierfish venom [77, 78]. Studies of bullrout venom, however, show its venom has no hyaluronidase or phospholipase activity and has no antigenicity with stonefish antivenom [80].

The envenomation from the lionfish is described as throbbing, but systemic signs or symptoms rarely occur [67]. Reviews of cases from North American poison centers show mild to moderate pain at the envenomation site, radiating up the affected extremity [66–68]. Local edema usually occurs, but vesicles and bullae formation are possible local effects of lionfish envenomation [66–68] (Fig. 13). Diaphoresis, chest or abdominal pain, and jaw tightness have occurred in a few cases [66, 67, 81].

Treatment

Treatment consists of basic first aid with immersion of the envenomated extremity in water as hot as can be tolerated without causing burns or scalding injury. This is to deactivate the heat-labile components of the venom. Hot water as high as 45 °C /113 °F has been used but can give rise to first degree burns. Therefore, water temperatures should not exceed 43 °C (Table 5). Recommended

Fig. 13 Vesiculation of the hand 48 h after the sting of a lionfish (Photo by Howard McKinney. From Ref. [133], p. 1495)

Fig. 14 Stonefish antivenom (Courtesy of John Williamson, MD. From Ref. [133], p. 1496)

immersion times range from 30 to 90 min. If recurrent pain occurs a repeat heat immersion can be tried. Appropriate level of analgesics should be given. Local or regional anesthetic blockade may be warranted, especially if embedded spines are present, and these need to be removed and the wound debrided and irrigated. Deeply penetrating spines especially in the soles of the foot or the palm of the hand may require surgical exploration and removal in the operating room. Radiographs to find retained foreign body are often needed. There is no support for the anecdotal use of folk remedies, meat tenderizer, antiseptics, or dyes to aid in local wound care. Cold immersion though should never be done. Antibiotics have been used as for any penetrating wound.

Stonefish antivenom is available in Australia through Commonwealth Serum Laboratories (CSL) of Australia (Fig. 14). It is indicated for severe envenomation. Each 2-ml vial contains 2000 units of equine-derived F(ab') [2] antivenom against *Synaceja trachynis*, but has been used for all stonefish envenomations. Dosing is based on the number of spinous puncture wounds as an approximation of venom load. If there are one or two puncture wounds, one vial of antivenom intravenously is recommended, if there are three or four puncture wounds then two vials can be used, and for cases with greater than four puncture wounds three vials have been used. If recurrent pain occurs, addition vials may be given [71]. Aquaria in other countries with stonefish may stock the antivenom even if unapproved locally. For example, major US aquaria that house these species may have the CSL antivenom for use with investigation new drug status. In the US consulting, the antivenom index may help locate which facilities carry the antivenom: (http://www.aza.org/antivenom-index/).

Envenomation by *Scorpaena* should be treated as stonefish envenomation with hot water immersion, pain control, local wound exploration with removal of spines, and ongoing wound care. Wound infections with *Vibrio vulnificus, Aeromonas Hydrophilia, Edwardsiella tarda, Streptococcus iniae, Erysipelothrix rhusiopathiae,* and *Mycobacterium marinum* have been associated with marine infections including necrotizing fasciitis [64].

The symptoms from lionfish envenomation can be treated with warm water immersion and analgesia alone (Table 5). Cold therapy can worsen symptoms and is to be avoided [66]. Stonefish antivenom, although demonstrated

in animal models to neutralize the cardiovascular effects of lionfish venom, is not used for these less symptomatic human envenomations [66, 78]. Wound exploration and radiographs to see if there is a retained spine may be needed [68], otherwise antibiotics should be reserved for cases which progress to cellulitis, lymphangitis, and tenosynovitis [66].

Catfish

Catfish are a diverse group of fish inhabiting both fresh and salt water environments. Notable for their barbels ("whiskers"), catfish lack scales, dwell at the bottom of rivers, lakes, streams and oceans, and may grow to 350 kg (*Pangasianodon gigas*). Eight families of catfish live underground, four families live in salt water. Some species of catfish have as many as four pairs of barbels (maxillary, nasal, and two chin), while others have none. The barbel is a special sensory organ, aiding in chemoreception and detection of food, and is not the organ responsible for envenomation. Catfishing is an important source of commerce, and important freshwater species include the channel catfish (*Ictalurus punctatus*), brown catfish *(Ictalurus nebulosus*), and black bullhead (*Ictalurus melas*).

All catfish, except the electric catfish, contain a hollow spine along their dorsal and pectoral fines. These three spines are covered with glandular tissue within an integumentary sheath and some contain barbed retrorse teeth [42]. The spines normally lie flat against the fin, but the animal may extend the spine in defense when it feels frightened. While the common route of envenomation is following puncture from one of these spines, there are reports of envenomation following handling of just the tail of some species (Arabian Gulf catfish and some Mississippi River species) [82, 83]. This is thought to occur through epidermal secretion of venom. Puncture wounds are more common than lacerations, though both occur. Hand injuries are commonly reported among those who handle catfish [82].

Pathophysiology

Catfish venom is species dependent, but in general, is a complex composition of hemolytic, dermonecrotic, and vasogenic proteins [84]. The potency is inversely proportional to the size of the fish [84]. When the integumentary sheath of the spine is broken, the heat-labile venom is injected into the wound. Crinotoxin, identified in *Arius thalassinus* and *Plotatus lineatus*, is secreted from the epidermis when the fish feels threatened and can enter humans through broken skin. Smooth muscle contraction and prostaglandin release are two effects from envenomation from crinotoxin. Salt water catfish have reputably more severe envenomations.

Clinical Presentation and Life-Threatening Complications

In general, there is little morbidity following catfish envenomations and death is a rare complication. The majority of injuries occur following handling of the fish. There can be lower extremity injuries from stepping on or brushing up against a catfish spine. In the case of *Arius thalassinus* and *Plotatus lineatus*, envenomation can occur from skin exposure to epidermally secreted toxin. The effects of catfish envenomation generally occur soon after the puncture or laceration from the spine. Pain may be intense and seemingly out of proportion to the exam and may extend centripetally. Left untreated, symptoms generally resolve within an hour. A robust inflammatory reaction leads to erythema, edema, local hemorrhage, and potentially skin necrosis [84]. Systemic findings, such as tachycardia, weakness, hypotension, nausea, vomiting, dizziness, paresthesias, loss of consciousness, and respiratory distress can occur, but are not common. Crinotoxicity is manifest by throbbing pain, tissue necrosis, and muscle fasciculations.

The major morbidity from catfish envenomation stems from secondary infections. Following injury from fresh water species, *Aeromonas hydrophila* inoculation is reported, while *Vibrio spp* infection

may complicate envenomation from salt water species [84]. Other infectious considerations include *Mycobacterium terrae*, *Corynebacterium spp*, *Staphylococcus* and *Streptococcus spp*. [82] as well as *Edwardsiella tarda*, *Klebsiella*, *Erysipelothrix*, *Nocardia*, *Chromobacterium, Sporothrix and Actinomyces* [84].

Diagnosis

There is no specific diagnostic test for catfish envenomations. Given the potential for spine dislodgement, routine use of radiographs seems appropriate to exclude foreign body. Secondary infections may resemble streptococcal cellulitis [82], though gram-negative cellulitis should be considered. Wound cultures may be a challenge to obtain given the small puncture size.

Treatment

There is no specific antidote for catfish envenomations. Treatment is primarily supportive and effectiveness may be time dependent. Hot water immersion is the most commonly utilized method to reduce pain. Catfish venom is heat-labile, and hot water immersion may inactivate venom proteins and limit local sequestration. Immersion in nonscalding water at 43 °C for 30–90 min or until analgesia is achieved is one approach (Table 5). Folk remedies such as pouring hot coffee over the wound, applying mineral salts, solvents, or other chemicals have no proven benefit. Another folk remedy, of doubtful value, is rubbing the wound with the gel-like material secreted from the skin of the traumatized fish. This is thought to act as a local vasoconstrictor and pain reliever. Local infiltration with an anesthetic such as lidocaine or bupivacaine may be a helpful adjunct.

Local wound exploration is paramount as retained spines may act as a source for infection and persistent pain. Radiographs are a reasonable adjunct to evaluate for a deeply penetrating spine or fracture. Like most puncture wounds or dirty lacerations, suturing should not be employed. Allowing the wound to heal by secondary intention is a more appropriate strategy. Tetanus prophylaxis is indicated in the previous unimmunized or if previous immunization is out of date. Careful observation and return for wound checks are important. Routine use of antibiotics empirically in high risks wounds (deeply penetrating hand or foot punctures) seems appropriate. Recommended oral regimens include ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole, or IV carbapenems or cefepime. For cellulitis associated with bullae, vesicles or ulcers where *Vibrio vulnificus* is suspected, IV ceftazidime, fluoroquinolones, plus doxycycline is recommended [64].

It is unlikely that ICU level care would be expected following a catfish envenomation. The most likely scenario would be sepsis in a susceptible host (immunocompromised or cirrhotic)

Amazonian Parasitic Catfish

Within the waters of the Amazon valley lives a strange creature with a reputation to swim into the urethra of unsuspected bathers, particularly during micturition. This catfish is known by several names including candiru, canero, vampire fish, toothpick fish, and urethra fish and is a member of the genus *Vandellia*. In addition to urethras, this transparent, parasitic fish has been reported to swim into vaginas, ears, noses, and anuses [85]. Adults may reach 40 cm (16 in.) in length, though most species are much smaller.

There is controversy regarding the legitimacy of human penetration by this fish, and the stories remained largely folklore over the last one hundred years. The fish has umbrella-like spines near its small head, which may extend and penetrate human tissue, thereby making removal difficult (much like the barb in some fish hooks). It naturally preys on fish, swimming against the stream into the gills of other fish where it attaches itself for a blood meal. Human "attacks" are likely accidental. While not venomous, the tissue damage and lacerations that occur from forceful

removal have been reported to cause death from massive hemorrhage [86].

Treatment

While penile amputations and forceful extractions are documented treatments for human exposures [86], prevention with tight fitting bathing suits may be a more practical approach. High-dose vitamin C and fresh juice from the unripen fruit of the jagua tree (*Genipa americana*) may be used by locals in remote settings as citric acid is reported to soften or dissolve the spines of the fish and facilitate removal. In modern health care settings, removal should involve a specialty trained surgeon (i.e., urologist). Unless severe hemorrhage or sepsis has occurred, ICU admission is unlikely.

Weeverfish

Nine species of weeverfish belong to the family *Trachinidae*, although a number of other fish are sometimes referred to as "weeverfish." The weeverfish has venomous spines located on its first 5–6 dorsal fins and gills. The name *weever* is from the Old French (*wivre, guivre, vivre*) for "viper." *Trachinus vipera* (the lesser weever) and *Trachinus draco* (the greater weever) are the most well-known. Other English names for the weever fish include adder pike, sea dragon, sea cat, black fin, scorpion fish, and stang. The weeverfish can reach up to 50 cm in length and are yellow-gray with a white belly. They are rugged animals, capable of surviving several hours out of water.

The weeverfish does not have a swim bladder. Therefore, it sinks to the bottom of the ocean when not actively swimming. Here, it buries itself under the sand and waits in ambush for unsuspecting prey to swim by. The spines of the weeverfish are associated with venom-containing glandular tissue. When the integrity of the glandular tissue is disrupted, after puncture, for example, venom is released through the spine and driven into the victim. The fish is easily provoked [87], but most injuries occur when the spines are accidentally stepped on by bathers or mishandled by fisherman. The lesser weeverfish is the most dangerous of all the weeverfish and is considered the most venomous of all fish in the temperate waters of the Eastern Atlantic, Mediterranean, Baltic, North, and Black Seas [87].

Pharmacology

The venom from the weeverfish is clear gray with an odor of ammonia. It contains several heat-labile, high molecular weight proteins, 5-hydroxytryptamine, and a protein responsible for releasing histamine in victim tissue, kinin-like proteins, and several catecholamines [88, 89]. *Trachinus draco* venom (dracotoxin) contains large amounts of catecholamines and histamine and has cholinesterase activity [90] and hemolytic properties [91]. Trachinine, one of the two lethal fractions from *T. vipera*, has been described as the most lethal venom ever derived from fish venom [87], but is labile and loses its toxicity after an hour at room temperature. Serotonin (5-HT) is found in the venom of other animals (cone snail, box jellyfish, Portuguese man-of-war, etc.) as well as the weeverfish and is potent pain-inducing substance.

Pathophysiology

Release of serotonin into the victim's tissue produces the characteristic pain associated with weeverfish envenomation. The histamine component is capable of producing wheal reactions, edema and erythema [87]. Central and autonomic system effects may be a sequela of the catecholamine component of venom.

Clinical Presentation and Life-Threatening Complications

Severe pain, immediately after the puncture, is the expected reaction. The pain, which is initially local, may radiate throughout the limb, becoming progressively more intense over about 30 min when symptoms peak. The pain has been

described as burning, crushing, stabbing, and "neuralgic" and can be out of proportion to the exam and difficult to control [87]. The pain generally resolves within 12 h, though may persist for up to a year [42]. Edema, erythema, cyanosis, and necrosis may be associated cutaneous findings. Systemic effects such as paresthesias, diaphoresis, convulsions, syncope, bradycardia, chest pain, respiratory distress, and delirium have been reported [87]. Weeverfish envenomation has been associated with spontaneous abortions [92]. Death is a rarely reported complication and may be from sepsis rather than a toxin-mediated process [93].

As with all puncture wounds, secondary bacterial infections can complicate the toxidrome. Gangrene, skin necrosis, and abscesses have been reported [87].

Diagnosis

There is no specific diagnostic test for weeverfish envenomations. Given the potential for spine dislodgement, routine use of radiographs seems appropriate to exclude foreign body. An accidental sting from a weeverfish should be in the differential diagnosis for any bather or fisherman who presents with severe pain and puncture wound if weeverfish are local species.

Treatment

There is no commercially available antidote for the treatment of weeverfish envenomations. The mainstay of treatment is geared toward analgesia. While the pain will generally resolve if untreated, the degree of pain can be severe. Immediate immersion in nonscalding hot water (43 °C) for approximately 30–90 min or until analgesia is obtained should be the initial treatment (Table 5). This may inactivate heat-labile proteins in the venom and limit local sequestration. Local anesthetic infiltration, for example, 1 % lidocaine without epinephrine, can be considered. Application of cold packs may worsen the pain and therefore should be avoided [88]. Intravenous calcium gluconate has been reported to help alleviate refractory pain [94]. While nonsteroidal anti-inflammatory drugs may be sufficient for pain relief, opiates would be a reasonable option if the pain is severe and refractory to hot water immersion. Anaphylaxis should be treated in the standard fashion.

Dislodgement of the spine is unusual, but radiography seems a reasonable tool to exclude spine foreign body. Local wound exploration and copious irrigation is important, though wide incision and drainage is not advocated given that this spine rarely breaks off into the victim and there is morbidity associated with further destruction of tissue [95]. Treatment for limb edema is probably best handled by elevation of the affected limb rather than pressure bandaging [95].

Tetanus prophylaxis is indicated in the previous unimmunized or if previous immunization is out of date. Prophylactic antibiotics should be considered in deeply penetrating wounds particularly in the hands or feet, though some have advocated that routine antibiotic use is unnecessary [96]. If antibiotics are to be used, consider coverage for *Vibrio spp* given the salt water environment.

Requirements for admission to an ICU are unusual following envenomation from a weeverfish, though consider this for situations where large doses of opiates are needed to control pain, anaphylactic reactions, secondary sepsis, or septic shock.

Starfish and Sea Cucumbers

Only one of the roughly 1,500 species of starfish is medically important. *Acanthaster planci*, the crown-of-thorns, is widely distributed in the Indo-Pacific Ocean, as well as tropical and subtropical zones of the Red Sea and the east coast of Africa across from the Indian Ocean. A known predator of coral, the crown-of-thorns starfish can decimate coral reefs [97]. *A. planci* is one of the largest sea stars, reaching diameters up to 60 cm, and is the only sea star which contains venom in its spines [98]. Injury occurs when one of the many spines of the sea star punctures and

penetrates human tissue; thus, it is important to wear protective gloves when handling them.

Sea cucumbers (*Synapta maculata*), members of the phylum Echinodermata, are found on the sea floor and have a worldwide distribution. They have a soft, elongated body and can reach upwards of 3 m. Several species are collected for aquarium habitats, while other species are cultivated for human consumption. While it would appear to be an easy target for prey, the sea cucumber contains holothurin, a neurotoxic substance to some marine organisms, and is also capable of ejecting a soap-like substance from its cloaca which can entangle would-be predators.

Pharmacology

Several in vitro experiments have demonstrated numerous effects of extracted *A. planci* venom. Venom components have demonstrated hemolytic, antiproliferative, apoptotic, edema-forming, and capillary permeability-increasing activity [99, 100]. Mice injected with lethal factor extract from *A. planci* have developed hepatocellular necrosis [101]. Holothurin A and B, produced by the sea cucumber, is a saponin which acts as an anionic surfactant. In isolated canine cardiac sarcolemmal vesicles, holothurin seems to interact with membrane permeability and can influence calcium and sodium exchange [102].

Clinical Presentation and Life-Threatening Complications

While *A. planci* is predacious to coral reefs, human envenomation is accidental, generally the result of mishandling or stepping on the sea star. Pain (ranging from mild to severe), erythema or discoloration, bleeding, and edema are the typical manifestations [103]. The pain is often self-limited and may last upwards of 3 h. While local symptoms predominant, systemic effects such as paresthesias, nausea/vomiting, and muscular paralysis may occur and are likely the result of multiple puncture wounds [42]. Subcutaneous granulomas and induration as well as tenosynovitis have been reported [42, 98]. To date, there is just one case of fatal anaphylactic shock which manifest within minutes following a single-puncture wound from *A. planci* [103].

Handling sea cucumbers without protective gloves may cause contact dermatitis [42]. The major risk from exposure to sea cucumber toxin is ocular injury which may cause severe conjunctivitis and blindness [42]. Holothurin is reported to cause severe illness or death if ingested [42]. All species of sea cucumbers are poisonous if ingested.

Diagnosis

There is no specific diagnostic marker for exposure to either the sea cucumber or sea star. Because spine fragmentation into soft tissue has been reported, x-rays following puncture wounds from *A. planci* is reasonable.

Treatment

Earlier reports suggest rapid and dramatic report of sudden collapse following *A. planci* envenomation; however, these are of questionable validity. Nevertheless, the priority for treatment following exposure to the crown-of-thorn sea star should be prompt removal/retreat from the aquatic environment. Once out of water, immediate immersion of the affected body part in hot, but nonscalding, water should take place until analgesia is obtained. Local anesthetics can be used for pain control if hot water immersion has failed to provide significant relief. Opiate analgesics may be useful for refractory pain. Surgical excision may be necessary for retained spines [98]. Repeated steroid injections (2 mg triamcinolone acetonide diluted fivefold with 1 % Xylocaine weekly) has been reportedly used for persistent subcutaneous induration from retained foreign bodies following *A. planci* envenomation. Anaphylaxis should be treated in the standard fashion.

The dermatitis from sea cucumber exposure can be treated with topical steroids or for severe reactions, systemic steroids [42]. Topical

analgesics may facilitate exam and irrigation. Careful inspection for any signs of a foreign body and, if there is suspicion of ocular exposure, fluorescein examination to exclude a corneal abrasion is indicated. Prompt ophthalmology referral is appropriate if there is ocular involvement. Though not well studied, cycloplegic, mydriatic, and corticosteroid ophthalmic solutions have been suggestive as treatments for inflammatory keratitis in the absence of appreciable infection [42].

Octopuses

All species of octopus are venomous; however, the most poisonous mollusca species are the southern blue-ringed octopus (*Hapalochlaena maculosa)* and greater blue-ringed octopus (*Hapalochlaena lunulata*) [71]. These are found in warm semi-tropical waters of the Pacific Ocean around Australia, New Zealand, the Philippines, and as far north as Japan, and in the Indian Ocean with distribution in New Guinea, Malaysia, and Sri Lanka [71].

These are small creatures, usually less than 20 cm long even with its tentacles extended, and tend to prefer a habitat of shallow water tide pools. They are usually not found deeper than 10 m of seawater. This habitat makes them easily found by sea bathers, curious children, snorkelers and shoreline divers. While at rest and undisturbed, they have bands that are a yellow color; however, when agitated the body darkens and its rings, which contain chromatophores, turn bright blue [104]. A typical blue-ringed octopus may have 50–60 such brightly colored rings. Unfortunately in this state they become more fascinating to children and adults unwary of its toxic potential (Fig. 15).

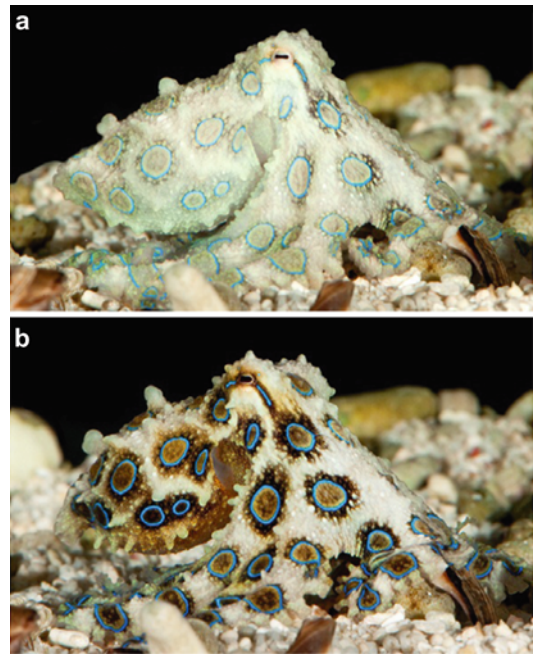

Fig. 15 Blue-ringed octopus (*H. lunulata*) with exposed *blue rings*, showing how varying states of expansion of chromatophores surrounding each ring can dramatically change the conspicuousness of the *blue rings* from relatively pale (**a**) to very conspicuous (**b**) (Photo by Roy Caldwell from: Ref. [104])

Pharmacology

The venom of the blue-ringed octopus contains tetrodotoxin, the same toxin found in puffer fish, the Oregon rough-skinned newt, and poison dart frogs. It is found throughout the blue-ringed octopus's body, but the venom delivery is via its salivary glands, and a strong ventral mouth and piercingly strong jaws [105]. They can inject their venom deep into muscle fascia. The purpose of the toxin is for the octopus to use to overcome its prey, usually crabs and shrimp, and with its' adjacent suckers can hold its food, while the tetrodotoxin is delivered via an injection through the skin. Other tissue spreading factors in the venom include hyaluronidase and vasogenic constituents such as histamine, tyramine, and serotonin. These substances may cause hypotension in experimental animals, but hypotension in human envenomation is not likely to occur.

Tetrodotoxin blocks peripheral voltage-gated sodium channels and produces rapid onset of weakness and paralysis in all motor nerves [42, 106]. Central nervous system effects are absent, and consciousness is maintained throughout in human victims.

Clinical Presentation and Life-Threatening Complications

The blue-ringed octopus does not envenomate while freely swimming. When a human gives the small blue-ringed octopus, a ride on an arm or hand the octopus can bite and envenomate [42]. This should never be done, unless the diver wears impermeable rubber gloves. At the bite site, usually two small puncture wounds are seen. Only minimal pain occurs at the time of the bite itself. Muscle aches and a stinging sensation ensue, followed by slight anesthesia at the bite site within 5–10 min. From the envenomation site, the sensations spread to the whole limb. Within a half hour, the bite site becomes red and swollen [42, 107–111]. Nausea, vomiting, hives, and itching all can occur. As the sodium channel blocking effect of the tetrodotoxin becomes systemic, perioral and tongue numbness occur. Subsequently, muscle weakness begins and can progress rapidly to complete paralysis. Bulbar palsies with diplopia, dysarthria, and blurred vision occur. Inability to stand and walk occurs as larger muscles are affected, and deep tendon reflexes are lost [42]. As the muscles of respiration are affected, chest tightness and breathlessness occur. Progression to respiratory failure, complete flaccid paralysis, and death may occur unless medical intervention is delivered [42, 110]. Pupils may dilate and become unreactive to light reflex, causing the physician to misdiagnosis brain death.

Treatment

Treatment includes rapid recognition of the effects of the blue-ringed octopus bite and summoning of advance first aid. Early mouth-to-mouth respiration or bag-valve-mask ventilation to preserve ventilation may be necessary. In rare cases, endotracheal intubation with ventilator management is required [108, 109]. The duration of venom effects is quite variable but may last up to 10–12 h [71]. Complete recovery may require a few days. Unfortunately there is no antitoxin or antidote. Wound care for the bite site is also important [111]. Granuloma annulare has occurred with other octopus bites [112]. A light pressure immobilization bandage to occlude lymphatic flow might temporize the systemic spread of the toxin until definitive airway skilled personnel arrive [42].

Indications for ICU admission are generally related to cardiovascular and nervous system effects and would include progressive muscular weakness, respiratory insufficiency/arrest, and significant alteration of mental status or cardiac dysrhythmias.

Cone Snails

On display in the Pergamon Museum in Berlin is a 5000-year-old necklace of cone shells excavated from a tomb in the Mesopotamian city of Uruk, proving that the attraction for these beautiful shells dates back centuries [113] (Fig. 16). The Conus species contains many beautiful appearing shells in which a living snail resides with an effective stinging apparatus for capturing its prey. Smaller Conus species feed on worms (vermivores) but are less toxic, while mollusk hunting (molluscivores) and fish-hunting (piscivores) are potentially toxic when they envenomate humans [113]. Over 700 individual Conus marine snails exist in the Conus species. While stings are rare, they are potentially fatal due to the unique and complex nature of the conotoxins in its venom [71, 114–122]. Most cases occur along the coastlines of the Pacific Ocean, and fatalities have mostly been due to *Conus geographus* [114, 115]. However, other Conus species are capable of a painful envenomation [71, 115] (Fig. 16).

Cone snails tend to burrow into the sand during the day and emerge at night to feed on fish or mollusks [71, 114]. The stinging apparatus of snail cones is shown in Fig. 15. The harpoon-like radular tooth is launched by the proboscis. Conotoxin venom is stored in the venom bulb which pumps it through the venom duct into the hollow barbed radular tooth. Since the snail itself is slow moving, this rapidly firing harpoon is

Fig. 16 Seven *Conus* species are shown. The large specimen at the extreme *left* is *Conus marmoreus*, the marble cone, the type species of the genus *Conus*, and at the extreme *right* is the geography cone, *Conus geographus*, the species causing the majority of human fatalities. The large specimen on *top* is the glory-of-the-sea cone, *Conus gloriamaris*, one of the most prized and valuable natural history objects of the eighteenth and nineteenth century. The four smaller shells on the *bottom* row are, from *left* to *right*, *Conus cedonulli*, the matchless cone, a specimen of which once outsold a masterpiece by Vermeer; *Conus imperialis*, the imperial cone; *Conus purpurascens*, the purple cone; and *Conus magus*, the magician's cone. *C. cedonulli* and *C. imperialis* are vermivorous (worm-hunting) species; *C. gloriamaris* and *C. marmoreus* are snail-hunting species; and *C. purpurascens*, *C. magus,* and *C. geographus* are piscivores (fish-hunting cone snails) (Photo from: Ref. [113])

effective at striking its prey, and the conotoxins secreted into its hollowed barbed tooth are effective at immobilizing it [71].

Pharmacology

The conotoxins are actually several hundred peptides, which share a disulfide bridge, but have great variation in their activity between species and even within the same species [113, 115–117]. The common mechanism of action is through ion channel blockade at different receptors including calcium, sodium, potassium, and acetylcholine channels (Table 4). Blockage of the nicotinic acetylcholine receptor subtype results in paralysis, usually only in the snail's prey, but human envenomation can produce diffuse muscle weakness. The alpha-conotoxin, which blocks neuromuscular acetylcholine receptors, is mechanistically similar in action to alpha-bungarotoxin. The mu-conotoxins, which block sodium channels, are mechanistically similar to tetrodotoxin and saxitoxin. Both of these produce neuromuscular paralysis. One conotoxin peptide, an omega-conotoxin derivative, from the species *Conus magus*, the magician's cone, has been developed into the pharmaceutical agent ziconotide, used for intrathecal injection for central neurologic pain control [116, 118, 119]. It blocks the N-type calcium channel [119]. Other nonconotoxin peptides lack a disulfide bond and have other physiologic actions (Table 4). The conopeptide conantokin-G was originally called the "sleeper peptide," as it put young mice into a trance like state, when injected directly into the CNS, via its blocking action on the NMDA receptor [113].

Clinical Presentation and Life-Threatening Complications

Human envenomation occurs when a diver handles the shell unaware it is home to the snail. Slight pressure on the proboscis causes the radular tooth to penetrate the skin and may break off. The initial pain is similar to a bee sting, but may include localized edema or cyanosis. Depending on the species involved, symptoms may be localized to pain, or spreading paresthesia with limb heaviness

Table 4 Physiologic actions of some conotoxins

Omega-conotoxin	Voltage-gated calcium channel N-type blockade
Mu-conotoxins	Voltage-gated sodium ion channel blockade
Delta-conotoxin Iota-conotoxin	Voltage-gated sodium ion channel enhancer
Kappa-conotoxins	Voltage-gated potassium ion channel blockade
Alpha-conotoxin Psi-conotoxin	Ligand-gated nicotinic acetylcholine receptor antagonists
Sigma-conotoxin	Serotonin receptor 5-HT3 blockade
Rho-conotoxin	Alpha-1 adrenoreceptor blockade
Chi-conotoxin	Noradrenaline transporter blockade
conantokin	NMDA (*N*-methyl D-aspartate) receptor blockade
conopressin	Vasopressin release modulator/agonist
contulakin	Neurotensin receptor agonist

or numbness, and constitutional symptoms such as nausea and malaise [120, 121]. Serious *Conus geographus* envenomations can cause generalized motor weakness, bulbar palsy symptoms (diplopia, ptosis, dysarthria, dysphagia, aphonia), respiratory arrest, coma, and cerebral edema [120, 122]. Death may occur if medical intervention is unavailable or delayed onset paralysis occurs with respiratory insufficiency. The severe effects can last for several hours and take a few weeks before complete recovery occurs [71, 122].

Treatment

Careful attention to respiratory support is essential for patients with paralytic symptoms. Intubation and ventilator support is critical once signs of diaphragmatic weakness and impending paralysis occur. As with other heat-labile venoms immersion of the envenomated limb in hot water up to 45 °C/113 °F may provide pain relief, but analgesics may also be necessary (Table 5). One source has recommended edrophonium, 2 mg IV as a test dose, similar to a tensilon test, with up to 10 mg IV in an adult, as a reversal agent for the neuromuscular blockade at the nicotinic acetylcholine receptor [71].

Table 5 Hot water immersion as initial treatment for Marine envenomation

Stingray	Sea Urchin
Stonefish	Scorpionfish
Lionfish	Blue-ringed Octopus
Cone snail	Weeverfish
Catfish	Starfish
Fire Coral Physalia	Crown-of-thorns

Indications for ICU admission are primarily related to neurologic or respiratory system effects and would include progressive weakness, respiratory insufficiency or arrest, coma, or significant altered mental status.

Sea Urchins

Roughly 950 species of sea urchins inhabit all the world's oceans but are often found among coral reefs. Most sea urchins have spines measuring upwards of 3 cm, though some may reach 30 cm. Spines are a defense mechanism for the sea urchin and act as a physical barrier capable of inflicting an uncomfortable puncture to predators.

Not all sea urchins are considered venomous, given only those in the family Diadematidae and Echinothuriidae have a venom apparatus. Venom is contained within the spines of the sea urchin or within pedicellaium, small clamp-like organs that can capture and hold onto prey (Fig. 17). Sea urchin spines can be broken after impaling humans, often as a result of mishandling or stepping on the creature. Regeneration of dislodged spines by the sea urchin is possible [123].

Pharmacology

Sea urchin venom contains several biologically active components including steroid glycosides, serotonin, hemolysin, protease and acetylcholine-like substances [124]. Cathepsin B/X, present in

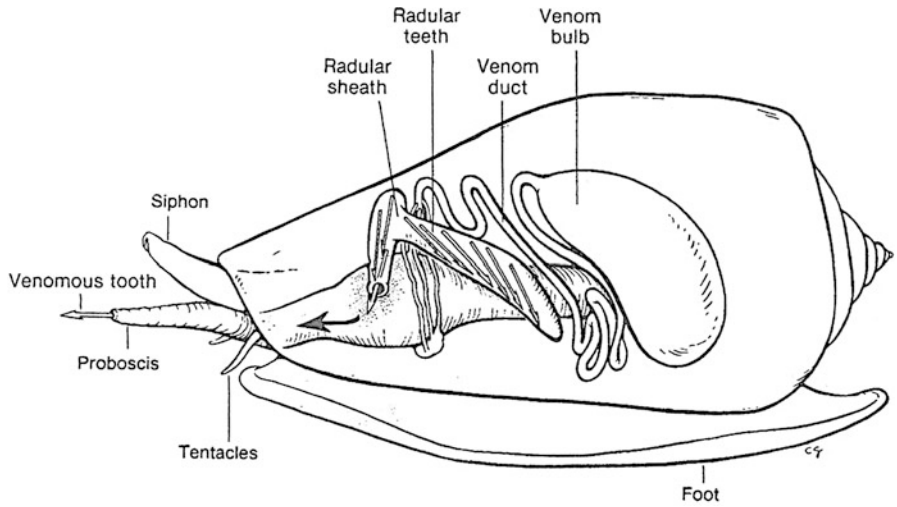

Fig. 17 Venom apparatus of the cone snail. (From Auerbach PS: Envenomation by aquatic invertebrates. In Auerbach PS [ed]: Wilderness Medicine, 4th ed. Philadelphia, Mosby, 2001, p 1481.)

the *Echinometra lucunter* sea urchin, is thought to contribute to the painful, inflammatory process following envenomation [123]. *Toxopneustes pileolus* causes histamine release from rat mast cells, whereas contractin A induces contraction of tracheal smooth muscle in guinea pigs [125, 126]. The venom of the Pacific *Tripneustes* urchin contains a neurotoxin that targets facial and cranial nerves [42].

Clinical Presentation and Life-Threatening Complications

Local inflammatory reactions, edema, local sensory loss, or pain are common features shortly following envenomation by sea urchins [127, 128] (Fig. 18). The pain associated with envenomation is moderate to severe in intensity and has been described as burning or aching. Spines may be visible underneath the skin and those from *Diadema setosum* or *Strongylocentrotus purpuratus* may appear purplish [129]. Systemic features including nausea/vomiting, abdominal pain, paresthesias, muscular paralysis, syncope, delirium, hypotension, and respiratory distress may occur but appear to represent a minority of cases [130]. Osteoarthritis, tenosynovitis, fasciitis, and bursitis were reported in a cases series of envenomations from Reunion Island [131]. Urchin granulomas may develop months after the injury [132]. Two cases involving multiple stings from a black sea urchin in Hawaii presented with bulbar polyneuritis and respiratory insufficiency 6–10 days after envenomation. One patient developed magnetic resonance imaging-documented meningoencephalitis, whereas the other had signs and symptoms mimicking Guillain-Barré syndrome, with hyporeflexia and elevated cerebrospinal protein levels [71]. Envenomation from the pedicellariae may cause more severe symptoms and, in addition to severe pain and the systemic features described above, aphonia, hypotension, and death [71].

Diagnosis

There is no specific diagnostic study in the management of sea urchin envenomation. Differential diagnosis would include envenomation from other stinging fish or simple punctures wound from nonvenomous animals, corals. Given the possibility of spine fragmentation, x-rays should be considered for all envenomations. Consider ultrasound, CT or MRI if negative x-rays but strong suspicion for embedded spine.

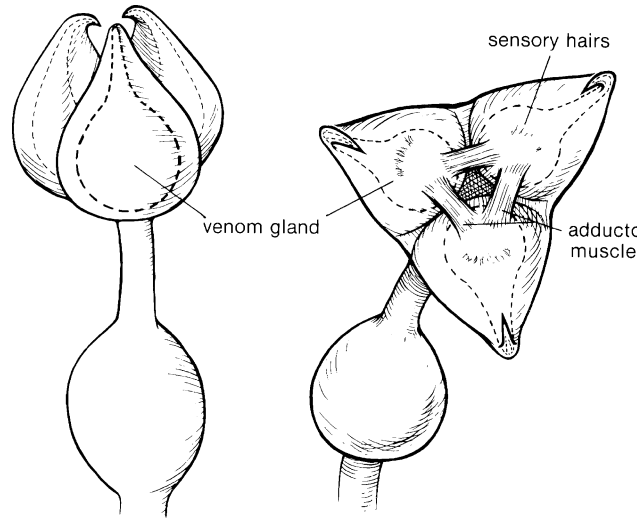

Fig. 18 Globiferous pedicellaria of a sea urchin, used to hold and envenom prey (From Ref. [133], p. 1476)

Fig. 19 Finger swelling from sea urchin puncture. A single spine entered the palm over the third metacarpal bone. Swelling was severe in the second and third digits (Photo by Paul Auerbach, MD. Courtesy of John Williamson, MD. From Ref. [133], p. 1478)

Treatment

There is no specific therapy or antidote for sea urchin envenomation. Treatment should begin with immediate hot water immersion (nonscalding) for 30–90 min or until anesthesia is achieved (Table 5). Easily reachable spines or pedicellaria should be removed as persistent envenomation may continue. Analgesics, including opiates in severe cases, should be considered. Presumptive wound exploration without evidence of spine fragmentation should be avoided, as spine localization is unlikely. Some species of sea urchins contain a dye that stains tissue and may confuse the practitioner for retained foreign body, though this dye should fade in 36 h.

Surgical consultation, by either an orthopedic, plastic, or general surgeon, is indicated for deeply penetrating spines that are causing persistent pain, synovitis, or are the source for infection. Splinting the affected structure to avoid further fragmentation may be beneficial. There is no consensus on the routine use of prophylactic antibiotics or anti-inflammatories in the management of these injuries. Tetanus prophylaxis should be instituted when applicable (i.e., previously unvaccinated or out of date) (Fig. 19).

Intervention	Organism	Level of evidence
Acetic acid 5 %	*C. fleckeri*	III
Stingose	*P. physalis*	III
Box Jellyfish Antivenom	*C. flexeri* *C. quadrigatus*	III
Magnesium sulfate	Carybdeid spp.	III
Hot water immersion	All stinging fish	III
Opiate analgesics	All painful envenomations	III
Stonefish antivenom	Synaceia spp.	III
Prophylactic antibiotics	All penetrating envenomations	III

(*continued*)

Intervention	Organism	Level of evidence
Surgical debridement	All penetrating envenomations	III
Corticosteroids	*Physalia spp.* *L. philippinus* *A. planci* *S. maculata*	III
Pressure immobilization	Hapalochlaena spp.	III
Edrophonium	*C. geographus*	III

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